A Study of COVID-19 Using Mathematical Modeling

A

Synopsis

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1.Introduction

Intermittent outbreaks of infectious diseases have had profound and lasting effects on societies throughout history. These events have powerfully shaped the economic, political, and social aspects of human civilization, with their effects often lasting for centuries. Epidemic outbreaks have defined some of the basic tenets of modern medicine, pushing the scientific community to develop principles of epidemiology, prevention, immunization, and antimicrobial treatments.

The world has suffered many epidemics and pandemics in past, most notable of which is-the outbreak of Black Death, or **bubonic plague** in 1347, the most lethal pandemic in history which mainly devastated Europe **[1]**.

The **Spanish flu** pandemic in the beginning of the twentieth century (1918-20) was the first true global pandemic and the first one that occurred in the setting of modern medicine, with specialties such as infectious diseases and epidemiology studying the nature of the illness and the course of the pandemic as it unfolded.

Severe Acute Respiratory Syndrome (SARS) was the first outbreak in the twenty-first century that managed to get public attention. Caused by the SARS Corona virus (SARS-CoV-2), it started in China and affected fewer than 10,000 individuals, mainly in China and Hong Kong, but also in other countries. Due to the vigilance of public health systems worldwide, the outbreak was contained by mid-2003.

The 2009 **H1N1 pandemic** was a reprise of the "Spanish flu" pandemic from 1918, but with far less devastating consequences. Suspected as a re-assortment of bird, swine, and human flu viruses, it was colloquially known as the "swine flu".

In December 2019 a type of pneumonia took place in Wuhan, a large city of Hubei province of central China. Very quickly it spread nationwide. The Chinese Center for Disease Control and Prevention (CCDC) identified a novel beta-coronavirus called 2019-nCoV, now officially known as **Severe Acute Respiratory Syndrome Coronavirus 2** (SARS-CoV-2). This was the third zoonotic coronavirus breakout in the first two decades of the 21st century, allowing human-to-human transmission and raising global health concerns. The world health organization was deeply concerned by the severity and global spread of the highly contagious disease and declared it a pandemic on March 11,2020. According to World Health 0rganization's 57th report on 17th March 2020; worldwide there have been 179,112

confirmed cases, with 7,426 deaths (about 4% mortality) **[2].** The World Health Organization's director-general Dr. Tedros Adhanom said that before World War Second, the world might not have seen such terrible sickness and emerging danger.

Till the date of 21st March 2021, Uttar Pradesh had recorded 6,07,050 confirmed COVID-19 cases, total 8,758 death cases, total 2,774 active cases and total 5,95,518 recovered cases. As per the records by 18th September, 2021 India has recorded 33,447,010 confirmed COVID-19 cases, including 447,166 (1%) deaths and total of 32,632,222 (99%) recovered cases.

As of 21st March 2022, Uttar Pradesh has recorded 20,70,285 confirmed COVID-19 cases, including 23,492 deaths, 778 active cases and 20,46,015 recovered cases. As per records, India has recorded a total of 4,29,84,348 confirmed COVID-19 cases as of 22nd March 2022, including 5,16,574 (1%) deaths and total of 4,24,67,774 (99%) cured cases **[3].**

Researchers have been making herculean effort worldwide to track and prevent the disease. They have been experimenting with innovative diagnostics and have developed vaccines in an attempt to contain the disease.

Mathematical models have the potential to trace and predict the epidemic trajectory under different circumstances. Epidemiologic mathematical models can help in predicting the epidemic peak in advance and analyse the impact of different factors in controlling its spread. The aim of this study is to propose a versatile model describing the epidemic flow which can be used in the local conditions of a city.

2. Literature Review

Various mathematical and statistical models have been proposed to understand the dissemination trajectory for a pandemic. Among these models, Susceptible (S)-Infected (I)-Recovered (R) model (SIR model) has been frequently used in the past to predict the dynamics of various contagious diseases i.e. HIV virus, plague, SARS. Recently, SIR models with different variations have been applied for prediction of COVID-19 trajectory and its epidemic peak in all over the world.

Pai et al.**[4]** investigated the COVID-19 transmission dynamics under the effect of lockdown. This study predicts that the peak of active infected cases around 43,000 will occur in the middle of May, 2020.

Sarkar et al.**[5]** proposed a six compartmental mathematical model i.e., susceptible (S), asymptomatic or pauci-symptomatic infected (A), symptomatic reported infected (I), unreported infected (U),

quarantine (Q), and recovered (R) ["SAIUQR" model] to predict the COVID-19 dynamics in four major states of India i.e. Jharkhand, Gujarat, Andhra Pradesh, and Chandigarh.

Tiwari et. al**[6]**proposed a five-compartment mathematical model i.e. Susceptible (S)-Exposed (E)-Infected (I)- Recovered (R)-Death (D) (SEIRD model) to analyze the progression and epidemic peak of COVID-19 pandemic using robust statistical methods i.e. linear regression method and least square method to estimate the SEIRD model parameters by analyzing publicly available reported data of COVID-19 outbreak in India. They have investigated the progression of COVID-19 and predict the epidemic peak under the impact of lockdown in India, where they examined the data (from January 30, 2020 to July 10, 2020 i.e,160 days) to enhance the accuracy of outcomes. Their results have been beneficial for determining further COVID-19 mitigation policies not only in India but globally as well.

In a study by Dhanwant et.al.**[7]** the authors have covered the analysis of the COVID-19 spread in different countries, and dealing the main feature of COVID-19 growth, that is the spread due to social-contact structure, which is governed by the infection rate. They found that the strictness at which social distancing in India is done, is insufficient for controlling the growth of COVID-19. In May 2020, Chatterjee et. al.**[8]** explored the infection of COVID-19 in India and a few other countries around the world by using SIRD model, where they made prediction regarding the peak rise at the end of June or beginning of July 2020 thereafter, the infection is expected to fall considerably from August.

Anwar Zeb et. al.**[9]**proposed a SEIQR model for the flow of COVID-19. In this study, a new mathematical model was proposed and analyzed to understand the transmission dynamics of the COVID-19 pandemic in Bangkok, Thailand. It is divided into seven compartmental classes, namely, susceptible, exposed, symptomatically infected, asymptomatically infected, quarantined recovered and death, respectively. The next-generation matrix approach was used to compute the basic reproduction number denoted as of the proposed model. The results show that the disease-free equilibrium is globally asymptotically stable if reproduction number is less than one. On the other hand, the global asymptotic stability of the endemic equilibrium occurs if reproduction number is greater than one. The mathematical analysis of the model is supported using numerical simulations. Moreover, the model's analysis and numerical results prove that the consistent use of face masks would go on a long way in reducing the COVID-19 pandemic**[10].**

Tang et. al.**[11]** proposed a simple mathematical model to explain the long duration of the pandemic COVID-19 in the 26 Brazilian states and their capitals. The model used cumulative total cases over a time. Analysis of the predicted number of new cases of COVID by the growth rate model and the total number of symptomatic patients admitted in hospitals, as well as the number of deaths related to COVID-19, was performed for Brazil and the five Brazilian regions (Southeast, South, Midwest, North, and Northeast) from the 8th (Feb 16–22) to the 44th (October 25–31) epidemiological week of 2020. Analysis of the predicted new cases was correlated with the total number of hospitalizations and deaths related to COVID-19.

Khajanchi et. al.**[12]** proposed and extended classical SEIR compartment model refined by contact tracing and hospitalization strategies to explain the COVID-19 outbreak. The model was calibrated with daily COVID-19 data for the five provinces of India namely, Kerala, Karnataka, Andhra Pradesh, Maharashtra, West Bengal and the overall India. To identify the most effective parameters a sensitivity analysis is conducted by using the partial rank correlation coefficients techniques. The value of those sensitive parameters are estimated from the observed data by least square method. The study demonstrates that a critically important strategy can be achieved by reducing the disease transmission coefficient and clinical outbreak rate to control the COVID-19 outbreaks. It also performed short-term predictions for the daily and cumulative confirmed cases of COVID-19 outbreak for five provinces of India and the overall India. Long-term predictions for the Republic of India revealed that the COVID-19 cases will exhibit oscillatory dynamics. The model simulation demonstrates that the COVID-19 cases across India at the end of September 2020 obey a power law.

Some important clinical studies related to COVID-19 helpful in finding the nature of the disease are as follows:

Liet.al.**[13]** studied the dynamics of early transmission of Novel Corona Virus Infected Pneumonia in Wuhan China. They observed that the mean incubation period of the disease was 5.2 days and estimated the basic reproduction number to be 2.2.

Kamph et. al.**[14]** reviewed 22 studies and observed that Syndrome (SARS) coronavirus, Middle East Respiratory Syndrome (MERS) coronavirus or endemic human coronaviruses (HCoV) can persist on inanimate surfaces like metal, glass or plastic for up to 9 days, but can be efficiently inactivated by

surface disinfection procedures with 62-71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite within 1 minute. Other biocidal agents such as 0.05-0.2% benzalkonium chloride or 0.02% chlorhexidine digluconate are less effective**.**

Bai et. al.**[15]**studied a cluster of five patients with COVID-19 pneumonia who came in contact with an asymptomatic relative and were infected. All patients underwent chest CT imaging. RT-PCR tests for COVID-19 nucleic acid were performed using nasopharyngeal swabs. The sequence of events suggested that the coronavirus may have been transmitted by the asymptomatic carrier.

Huang et. al.**[16]** studied 41 admitted hospital patients who had been identified as having laboratory-confirmed 2019-nCoV infection. They found that Most of the infected patients were men (30 [73%] of 41); less than half had underlying diseases (13 [32%]), including diabetes (eight [20%]), hypertension (six [15%]), and cardiovascular disease (six [15%]). Median age was 49·0 years (IQR 41·0-58·0). 27 (66%) of 41 patients had been exposed to Huanan seafood market. Common symptoms at onset of illness were fever (40 [98%] of 41 patients), cough (31 [76%]), and myalgia or fatigue (18 [44%]); less common symptoms were sputum production (11 [28%] of 39), headache (three [8%] of 38), haemoptysis (two [5%] of 39), and diarrhoea (one [3%] of 38). Dyspnoea developed in 22 (55%) of 40 patients (median time from illness onset to dyspnoea 8·0 days [IQR 5·0-13·0]). 26 (63%) of 41 patients had lymphopenia. All 41 patients had pneumonia with abnormal findings on chest CT. Complications included acute respiratory distress syndrome (12 [29%]), RNAaemia (six [15%]), acute cardiac injury (five [12%]) and secondary infection (four [10%]). 13 (32%) patients were admitted to an ICU and six (15%) died. Compared with non-ICU patients, ICU patients had higher plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNFα.

WHO proposed guidelines for implementation of Global surveillance of COVID-19 **[17].**

Harapana et. al.**[18]**conducted a literature review of publicly available information to summarize knowledge about the pathogen and the current epidemic. In this study, the causative agent, pathogenesis and immune responses, epidemiology, diagnosis, treatment and management of the disease, control and preventions strategies are all reviewed.

3. Preliminaries and Notations

i. Reproduction number (Ro)

One of the most important numbers in epidemiology is the basic reproduction number, Ro, defined as the expected number of infections directly generated by one case in a population in which all are susceptible to infection Ro can be estimated by fitting the data on reported infections to a Susceptible-Infectious-Removed-Deaths (SIRD) model**[19].**

The attack rate or transmissibility of a virus is indicated by its reproduction number, which represents the average number of people to which a single infected person will transmit the virus. On January 23rd, 2020, WHO's estimated Ro was between 1.4 and 2.5**[20]**. For comparison, the Ro for the common flu is 1.3 and for SARS it was 2.0. For $R_0>1$, the number of infected is likely to increase; for $R_0<1$, transmission is likely to decline and die out**[21].**

ii. **Case Fatality Rate (CFR)** - Percent of cases that result in death.

The novel coronavirus' case fatality rate has been estimated at around 3%, in the WHO press conference held on January 29, 2020 **[22].** For comparison, the case fatality rate for SARS was 10%, and for MERS 34%.

iii. **Incubation Period (how long it takes for symptoms to appear)**

COVID-19 Coronavirus Incubation Period Symptoms of COVID-19 may appear in as few as 2 days or as long as 14 during which the virus is contagious.

iv. Age and conditions of Coronavirus cases

Emerging COVID-19 incidence and outcome data indicate that men, especially older men, may also be more affected about 80% of those who died were over the age of 60 and 75% of them had pre-existing health conditions such as cardiovascular diseases and diabetes. 71% of cases were male. People of all ages can be infected by the novel coronavirus COVID-19. Older people, and people with pre-existing medical conditions (such as asthma, diabetes, heart disease) appear to be more vulnerable to becoming severely ill with the virus.

v. Zoonotic

A zoonosis (plural zoonoses or zoonotic disease) is an infectious disease caused by a pathogen (an infectious agent, such as a bacterium, virus, parasite or prion) that has jumped from an animal (usually a vertebrate) to a human.

vi. SIR Model

SIR model is the simplest model used in epidemic/pandemic studies which is expressed by a set of consequence ordinary differential equations (ODE) introduced by **Kermack** and **McKendrick[23].** The three differential equations represent susceptible (S) cases, active infected cases (I), and removed cases (R) including recovered and death **[24]**.

Furthermore, it is assumed that the time scale of the SIR model is short enough so that births and deaths (other than deaths caused by the virus) can be neglected and that the number of deaths from the virus is small compared with the living population. Based on these assumptions and concepts, the rates of change of the three populations are governed by the following system of ODEs.

$N = S + R + I$ **= Constant**

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \alpha I$$

$$\frac{dR}{dt} = \alpha I$$

where β is the infection rate and α is the recovery rate.

vii. SIRD model

The SIRD model includes one more equation on the number of deaths (D). The following set of Equations describes a comprehensive picture of the SIRD epidemic evolution **[18]**. In the SIRD model, total population N is considered as constant.

$N = S + R + I + D$ **= Constant**

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \alpha I - \gamma I$$

$$\frac{dR}{dt} = \alpha I$$

$$\frac{dD}{dt} = \gamma I$$

where α is the recovery rate, β is the infection rate, γ is the death rate,$\frac{dS}{dt}$ is the rate of change of susceptible people, $\frac{dI}{dt}$ is the rate of change of affected people, $\frac{dR}{dt}$ is the rate of change in the recovered people.

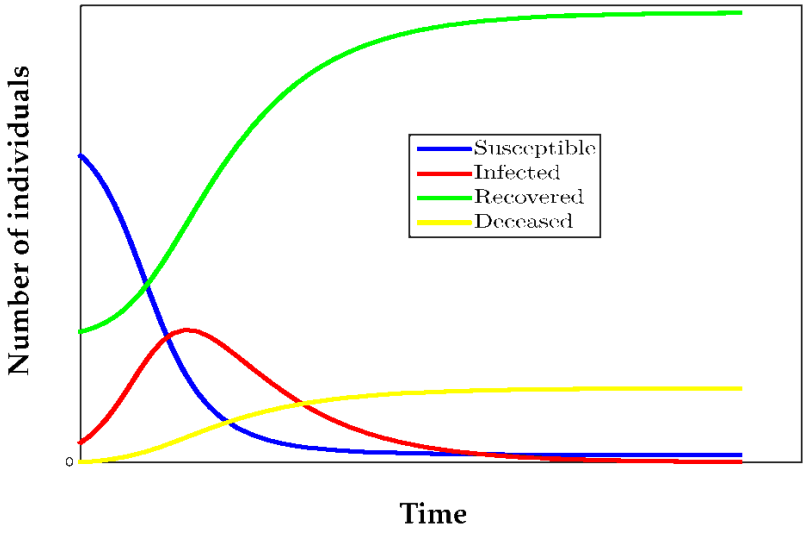

Figure 3. Typical behavior of an epidemic's evolution over time.

Figure 3 shows the usual way in which the variables S, I, R, and D evolve. No ranges appear, because they depend on each particular epidemic.

4. Lacuna in the past studies

From the literature review it was observed that the mathematical models proposed so far have not considered the following factors:

a) The variation in the rate of infection due to the change in the administrative policies like imposing lock down and removing it.

b) Reinfection of some people due to low immunity.

c) The reduction in infected population due to vaccination.

d) The effect of lockdown, vaccination and awareness on reproduction number R_0.

5. Proposed Study

In this study we propose to analyze the flow of COVID-19 under three different conditions.

In the following models S stands for susceptible, I stand for infected and $\tilde{\mathcal{R}}$stands for recovered or dead people. N, the total population of the region is assumed to be constant in each model.β is the coefficient for infection, α is the coefficient for recovery.

Modeling Time Dependent Infection Rate

Before vaccination was introduced.

When lock down was imposed in a periodic manner during weekends.

$$\frac{dS}{dt} = -\beta(t)SI + \delta\tilde{\mathcal{R}}$$

$$\frac{dI}{dt} = \beta(t)SI - \alpha I$$

$$\frac{dR}{dt} = \alpha I - \delta\tilde{\mathcal{R}}$$

At t = 0, S = $S_0 \geq 0$, I = $I_0 \geq 0$, $\tilde{R} = \tilde{\mathcal{R}}_0 \geq 0$

Plausible Rates of Infection

(ii) $\beta(t) = \beta_0 + aX(t)$, $\beta(t) \geq 0$

$$\ddot{X}(t) + \omega^2 X(t) = 0, X(0) = 0, \dot{X}(0) = \omega$$

(ii) $\beta(t) = \beta_0 - aX^2(t)$, $\beta(t) \geq 0$

$$\ddot{X}(t) + \omega^2 X(t) = 0, X(0) = 0, \dot{X}(0) = \omega$$

(iii)$\beta(t) = \begin{cases} \beta_0, & 0 \leq t \leq t_1 \\ \beta_1, & t_1 \leq t \leq T \end{cases}$, $0 < t_1 < T$, $\beta(t) = \beta(t+T), \beta(t) \geq 0$

N = S+I+$\tilde{\mathcal{R}}$= constant

δ is the coefficient for reinfection of the recovered people.

It is assumed that some of the recovered people who had low immunity are getting infected again.

Modeling Effect of Vaccination

After Vaccination has started.

$$\frac{dS}{dt} = -\beta SI - (1-\mu)V_0 \quad 0 \leq \mu \leq 1$$

$$\frac{dI}{dt} = \beta SI - \alpha I$$

$$\frac{d\tilde{R}}{dt} = \alpha I$$

$$\frac{dV}{dt} = \begin{cases} V_0, & V < S \\ 0, & V \geq S \end{cases}$$

At t = 0, S = $S_0 \geq 0$, I = $I_0 \geq 0$, $\tilde{R} = \tilde{R}_0 \geq 0$, $V \geq 0$

$$N = S+I+\tilde{\mathcal{R}} + (1-\mu)V$$

$\frac{dV}{dt}$ is the rate of vaccination. μ is the coefficient for reinfection of vaccinated people. V is the vaccinated population, V_0 is the constant rate of vaccination.

Modeling Effect of Awareness and Preventive Measures

The role of awareness of personal preventive measures like use of mask, head gear, medication and sanitization.

S = η S+(1-η)S, $0 \leq \eta \leq 1$

$$\frac{dS}{dt} = -\beta_1 \eta SI - \beta_2(1-\eta)SI + \delta\tilde{R}$$

$$\frac{dI}{dt} = \beta_1 \eta SI + \beta_2(1-\eta)SI - \alpha I$$

$$\frac{d\tilde{R}}{dt} = \alpha I - \delta\tilde{R}$$

At t = 0, S = $S_0 \geq 0$, I = $I_0 \geq 0$, $\tilde{R} = \tilde{\mathcal{R}}_0 \geq 0$

Here η S represents aware population and (1- η)S represents unaware population.β_1 and β_2 are the coefficient of infection for aware and unaware populations respectively and δ is the coefficient for reinfection of the recovered people.

6. <u>Outcome of the Study</u>

This mathematical model will provide analytical criteria to check the following:

a) Criteria for stability of the population.

b) Effect of various parameters like vaccination and awareness on the recovery rate of population.

c) Future prediction and visualization in varying conditions through data analysis methods and simulation technique.

7. <u>Purpose of the study</u>

1. To derive a mathematical model representing dynamics of COVID-19 spread.
2. To find the role of changing infection rate on the disease flow.
3. To find the role of reinfection of a fraction of population due to low immunity on the disease flow.
4. To find the effect of lockdown, vaccination and awareness on reproduction number R_0.
5. To form a simulation model for predicting the disease under different circumstances.

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